

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/618,380B

DATE: 09/22/2003

TIME: 11:06:09

Input Set : A:\058820176CNUS03.txt

Output Set: N:\CRF4\09222003\I618380B.raw

```
3 <110> APPLICANT: Weiner, George
        Gingrich, Roger
 5
        Link, Brian
        Tso, J. Yun
 8 <120> TITLE OF INVENTION: HUMANIZED ANTIBODIES AGAINST CD3
10 <130> FILE REFERENCE: 05882-0176-CNUS03
12 <140> CURRENT APPLICATION NUMBER: US 09/618,380B
13 <141> CURRENT FILING DATE: 2000-07-18
15 <150> PRIOR APPLICATION NUMBER: US 08/397,411
16 <151> PRIOR FILING DATE: 1995-03-01
18 <150> PRIOR APPLICATION NUMBER: US 07/859,583
19 <151> PRIOR FILING DATE: 1992-03-27
21 <160> NUMBER OF SEQ ID NOS: 14
23 <170> SOFTWARE: PatentIn version 3.1
25 <210> SEQ ID NO: 1
26 <211> LENGTH: 107
27 <212> TYPE: PRT
28 <213> ORGANISM: Artificial Sequence
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30 <220> FEATURE:

31 <223> OTHER INFORMATION: Light chain of Humanized 1D10 Ab minus signal sequence

45

33 <400> SEQUENCE: 1

35 Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly

10

39 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr

20 25

43 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Val

40

47 Ser Asn Ala Lys Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly

100

51 Ser Gly Ser Gly Lys Gln Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro

75 70

55 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His His Tyr Gly Asn Ser Tyr

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59 Pro Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys

63 <210> SEQ ID NO: 2

64 <211> LENGTH: 107

65 <212> TYPE: PRT

60

66 <213> ORGANISM: Mus sp.

68 <400> SEQUENCE: 2

70 Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly

5

74 Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr

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```
75
              20
                                  25
78 Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu Leu Val
82 Ser Asn Ala Lys Thr Leu Ala Glu Gly Val Thr Ser Arg Phe Ser Gly
86 Ser Gly Ser Gly Lys Gln Phe Ser Leu Lys Ile Asn Ser Leu Gln Pro
                      70
                                          75
90 Glu Asp Phe Gly Asn Tyr Tyr Cys Gln His His Tyr Gly Asn Ser Tyr
                  85
                                      90
94 Pro Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
              100
98 <210> SEQ ID NO: 3
99 <211> LENGTH: 116
100 <212> TYPE: PRT
101 <213> ORGANISM: Artificial Sequence
103 <220> FEATURE:
104 <223> OTHER INFORMATION: Heavy chain of Humanized 1D10 Ab minus signal sequence
106 <400> SEQUENCE: 3
108 Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
112 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr
    20
                                   25
116 Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Ile
                               40
120 Gly Val Lys Trp Ser Gly Gly Ser Thr Glu Tyr Asn Ala Ala Phe Ile
           55
124 Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Ser Leu
128 Lys Leu Asn Ser Leu Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
       85
                                       90
132 Arg Asn Asp Arg Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
136 Thr Val Ser Ser
          115
140 <210> SEQ ID NO: 4
141 <211> LENGTH: 116
142 <212> TYPE: PRT
143 <213> ORGANISM: Mus sp.
145 <400> SEQUENCE: 4
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151 Ser Leu Ser Ile Thr Cys Thr Gly Ser Gly Phe Ser Leu Thr Asn Tyr
155 Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Leu
159 Gly Val Lys Trp Ser Gly Gly Ser Thr Glu Tyr Asn Ala Ala Phe Ile
163 Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Phe
```

164 65



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167 Lys Met Asn Ser Leu Gln Ala Asp. Asp Thr Ala Met Tyr Tyr Cys Ala 85 90 171 Arg Asn Asp Arg Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val 172 105 100 175 Thr Val Ser Ser 176 115 179 <210> SEQ ID NO: 5 180 <211> LENGTH: 214 181 <212> TYPE: PRT 182 <213> ORGANISM: Artificial Sequence 184 <220> FEATURE: . 185 <223> OTHER INFORMATION: Complete light chain of Humanized 1D10 Ab 187 <400> SEQUENCE: 5 189 Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly 193 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr 197 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Val 35 40 201 Ser Asn Ala Lys Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly 55 205 Ser Gly Ser Gly Lys Gln Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 206 65 70 75 209 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His His Tyr Gly Asn Ser Tyr 213 Pro Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala 214 100 217 Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly 115 120 221 Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140 225 Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln 150 155 229 Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser 165 170 233 Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr 180 185 237 Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser 195 200 205 241 Phe Asn Arg Gly Glu Cys 210 245 <210> SEQ ID NO: 6 246 <211> LENGTH: 273 247 <212> TYPE: PRT 248 <213> ORGANISM: Artificial Sequence 250 <220> FEATURE: 251 <223> OTHER INFORMATION: Fd-jun in F(ab'-zipper)2 of humanized 1D10 antibody 253 <400> SEQUENCE: 6 255 Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu 🕑



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256	1				5				•	10					15		
		Leu	Ser	Leu		Cvs	Thr	Val	Ser		Phe	Ser	Leu	Thr	Asn	Tyr	
260				20		-			25	_				30		-	
263	Gly	Val	His	Trp	Val	Arg	Gln	Ser	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Ile	
264	_		35	-				40		_	_	_	45		_		
267	Gly	Val	Lys	Trp	Ser	Gly	Gly	Ser	Thr	Glu	Tyr	Asn	Ala	Ala	Phe	Ile	
268	-	50	-	-		-	55			•	-	60					
271	Ser	Arq	Leu	Thr	Ile	Ser	Lys	Asp	Thr	Ser	Lys	Asn	Gln	Val	Ser	Leu	
272		_				70	-				75					80	
275	Lys	Leu	Asn	Ser	Leu	Thr			Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	
276	-4				85				•	90	•		-	-	95		
	Arq	Asn	Asp	Arq	Tyr	Ala	Met	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val	
280	_		•	100	-			•	105	-	_			110			
283	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala	
284			115					120	-				125				
	Pro	Ser	Ser	Lvs	Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	Leu	Gly	Cys	Leu	
288		130		4			135	•	_			140		_	-2		
291	Val		Asp	Tvr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly	
	145		-	-		150					155		-			160	
295	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	
296					165										175		
299	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu	
300	_		-	180					185					190			
303	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro	Ser	Asn	Thr	
304	_		195		-		-	200				-	205				
307	Lys	Val	Asp	Lys	Lys	Val	Glu	Pro	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr	
308	-	210	-	-	-		215		_		-	220	_				
311	Cys	Pro	Pro	Cys	Lys	Cys	Pro	Ala	Gly	Gly	Arg	Ile	Ala	Arg	Leu	Glu	
	225			_	_	230			_	_	235			_		240	
315	Glu	Lys	Val	Lys	Thr	Leu	Lys	Ala	Gln	Asn	Ser	Glu	Leu	Ala	Ser	Thr	
316		_			245					250					255		
319	Ala	Asn	Met	Leu	Arg	Glu	Gln	Val	Ala	Gln	Leu	Lys	Gln	Lys	Val	Met.	
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323	Asn																
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330	<213	3> OI	RGAN:	[SM:	Art	ific	ial S	Seque	ence								
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333	<223> OTHER INFORMATION: Complete heavy chain of Humanized 1D10 Ab																
335	5 <400> SEQUENCE: 7																
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338	1 .				5					10					15		
341	Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser	Gly	Phe	Ser	Leu	Thr	Asn	Tyr	
342				20					25					30			
345	Gly	Val	His	Trp	Val	Arg	Gln	Ser	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Ile	
346			35					40					45				
349	Gly	Val	Lys	Trp	Ser	Gly	Gly	Ser	Thr	Glu	Tyr	Asn	Ala	Ala	Phe	Ile	
350		50					55					60					



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						•										
353 354		Arg	Leu	Thr	Ile	Ser 70	Lys	Asp.	Thr	Ser	Lys 75	Asn	Gln	Val	Ser	Leu 80
		I.e.ii	Asn	Ser	T.e.11		Δla	Δla	Asn	Thr	_	Val	Tyr	Tur	Cvs	
358	Lyo	nc a	11511	UCI	85	1111	1114	1114	тор	90	111.0	, 41	- 7 -	- 7 -	95	
	Δra	Aen	Aen	Δra		Δla	Mot	Aen	Tur		Glv	Gln	Gly	Thr		Val
362	Arg	Moli	nsp	100	тут	лια	Mec	лор	105	ттр	Gry	GIII	Gry	110	пса	VUI
	Thr	17-1	C0.x		717	802	Th ν	Tuo		Dro	802	17 n 1	Phe		Lou	Λla
366	TIIL	vai	115	ser	мта	Ser	TIII	120	GTĀ	FIO	Ser	val	125	FIU	neu	Ата
	Dwo	C 0 20		T	C02	Th∽	C0~		C1.,	Thr	71.	ת ו ת		C1 11	Cvc	LOU
	PIO		ser	ьуѕ	ser	THE		вту	сту	IIII	Ата		Leu	СТУ	Cys	neu
370	T7_ 7	130	71	Ш	Dh.	D	135	Dwa	17.5.1	mb ~	77.0.7	140	П~~	7 00	Cor	C1
374		гуу	Asp	ıyı	Pne	150	GIU	PIO	vaı	1111	155	Ser	Trp	MSII	ser	160
		T	mh sa		C1	•	111.0	mba	Dho	Dwo		17-1	T 011	Cln	202	
	Ата	ьeu	Inr	ser.	_	vai	HIS	THE	Pne		ATa	vaı	Leu	GIII		ser
378	01	T	m	0	165	0	C	77- 7	77- 3	170	77 n 7	D	C =	C = 10	175	T 0
	GTÀ	ьeu	Tyr		Leu	Ser	ser	val		Thr	vaı	Pro	Ser		ser	Leu
382	0.1	ml.	<b>01</b> -	180	m	<b>T1</b> .	<b>~</b>	7	185	7	11.7 -	T	D	190	7	mh
	GTA	Thr		Tnr	Tyr	тте	Cys		vaı	Asn	HIS	гуѕ	Pro	ser	ASI	Thr
386	_		195	_	_		<b>~</b> 1	200	_	~	^	<b>.</b>	205	m\	77.2	ml
	ьуs		Asp	ьys	гàг	vaı		Pro	ьys	Ser	Cys		Lys	Tnr	HIS	Thr
390	_	210	_	_	_		215	~ 1	_	_	- 1	220	_	_		<b>D</b> 1
	_	Pro	Pro	Cys	Pro		Pro	GLu	Leu	Leu		GTŻ	Pro	Ser	vaı	
	225		_	_	_	230	_	_		_	235		_	_		240
	Leu	Phe	Pro	Pro		Pro	Lys	Asp	Thr		Met	lle	Ser	Arg		Pro
398				_	245			_		250		~ .	_	_	255	
	Glu	Val	Thr	_	Val	Val	Val	Asp		Ser	His	GLu	Asp		GIu	Val
402	_		_	260			_		265				_	270	_	m1
	Lys	Phe		Trp	Tyr	Val	Asp	_	Val	Glu	Val	His	Asn	Ala	Lys	Thr
406	_	_	275			_,	_	280	_		_	_	285		^	
	Lys		Arg	GLu	Glu	GIn	_	Asn	Ser	Thr	Tyr	_	Val	Val	Ser	val
410	_	290		_		- 1	295	_	_	_	~ 1	300	<b>~</b> 1	_	-	_
		Thr	Val	Leu	His		Asp	Trp	Leu	Asn		Lys	Glu	Tyr	гàг	
	305			_	-	310		-		_	.315	<b>0</b> 3		m)	<b>-</b> 1 -	320
	Lys	Val	Ser	Asn	_	Ala	Leu	Pro	Ата		тте	GIU	Lys	Thr		ser
418	_		_	6.3	325	_	_	~ 3	_	330			m)	Ŧ	335	D
	Lys	Ala	гуѕ	_	GIn	Pro	Arg	GLu		GIn	vaı	Tyr	Thr		Pro	Pro
422	_	_	_	340	_	m)	_	_	345		_	-	m)	350	<b>.</b>	**- 1
	Ser	Arg	_	GLu	Leu	Thr	Lys		Gin	vaı	Ser	Leu	Thr	Cys	Leu	vaı
426	_		355	_	_	_	_	360	- 1			_	365	_	_	<b>61</b>
	Lys		Phe	Tyr	Pro	Ser		тте	Ala	vaı	GIU		Glu	Ser	Asn	GTÀ
430		370	~ 1	_	_	-	375	m)		_	_	380	<b>-</b>		^	70
		Pro	GLu	Asn	Asn		гàг	Thr	Thr	Pro		vaı	Leu	Asp	Ser	
	385	_			_	390	_		_		395	_	_	_	_	400
	GLy	Ser	Phe	Phe		Tyr	Ser	Lys	Leu		Val	Asp	гàг	Ser		Trp
438					405		_	_	_	410			~ 1		415	
	Gln	Gln	Gly		Val	Phe	Ser	Cys		· Val	Met	His	Glu		Leu	His
442	_		_	420		_	_	_	425	_	_	_		430		
	Asn	His	_	Thr	Gln	Lys	Ser	_	Ser	Leu	Ser	Pro	Gly	Lys		
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## Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:14; Xaa Pos. 2,3,4,5,6,7